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Klinefelter Syndrome with Poor Risk Extragonadal Germ Cell Tumor

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ABSTRACT

Germ cell tumors are the most common malignancy in men aged 15-35 years old, with a small percentage presenting in an extragonadal location. These tumors are seldom identified in the gastrointestinal tract. There is increased risk of extragonadal germ cell tumors (EGCT) in men with Klinefelter syndrome (KS). We report a rare case of a 37-year-old male with KS and EGCT discovered in the duodenum and pelvis. After treatment with Bleomycin-Etoposide-Cisplatin (BEP), he developed growing teratoma syndrome (GTS) and myelodysplasia. Despite surgical excision of the pelvic growing teratoma, he unfortunately died secondary to complications of severe bone marrow suppression.

Introduction

Germ cell tumors are the most common malignancy in the testicle, and the most common malignancy in males 15-35 years old.[1] It is reported that 5% of germ cell tumors are extragonadal.[1] Men with Klinefelter syndrome (KS) have an increased risk of developing extragonadal germ cell tumors (EGCT), though the overall risk has not warranted routine screening in the KS population.[2] The most common primary site of EGCT is the mediastinum, followed by the retroperitoneum.[1] Literature has described cases of EGCTs located in the pineal gland, presacral area, bladder, prostate, and liver.[1] To our knowledge, there has never been a published case of EGCT of gastrointestinal origin. We report a case of a patient with KS and EGCT of duodenal origin.

Case presentation

A 37-year-old male presented with nausea, vomiting, abdominal pain, weight loss, and symptoms of gastroesophageal reflux disease despite medical management. Computed tomography (CT) demonstrated a 16 cm distal gastric mass and a 7 cm pelvic mass (Fig. 1A–C). Biopsy of the gastric mass was nondiagnostic. Esophagogastroduodenoscopy identified a mass at the distal pyloric region of the stomach suggestive of a hemangioma, but was not biopsied due to concern for bleeding. An exploratory laparotomy was performed with resection of abdominal mass, partial gastrectomy, partial hepatectomy, and a roux-en-y gastroduodenostomy. Pathologic analysis demonstrated mixed germ cell tumor with components of immature teratoma and yolk sac tumor, consistent with extragonadal nonseminomatous germ cell tumor (NSGCT). The patient was referred to Louisiana State University Department of Urology for further evaluation. On physical examination, he was tall with long limbs, and had bilaterally descended small atrophic testicles with no masses. Tumor markers were: β-hCG 13 (<5), AFP 10511 (<15), and LDH 247 (<201). Karyotype was performed, which diagnosed Klinefelter syndrome (47 XXY). A scrotal ultrasound revealed small (<1 cc) testes bilaterally with no masses. Staging CT of the chest, abdomen, and pelvis was significant for an 8.4 × 7.0 × 5.6 cm pelvic mass, mild right hydroureteronephrosis, bilateral pelvic lymphadenopathy >1 cm, T11 vertebral body fracture, and mediastinal lymphadenopathy >1 cm. Magnetic resonance imaging (MRI) of the brain was negative for metastasis. Bone scan was performed, which demonstrated a T11 lytic lesion concerning for pathologic compression fracture (Fig. 2). This staged the patient as cTxN1M1bS3 nonseminomatous EGCT, Stage IIIC, with poor prognostic features. The patient was treated with four cycles of Bleomycin-Etoposide-Cisplatin (BEP) chemotherapy per NCCN guidelines. Tumor markers, repeated after chemotherapy, had normalized. Postchemotherapy imaging demonstrated disease progression despite chemotherapy, with interval progression from

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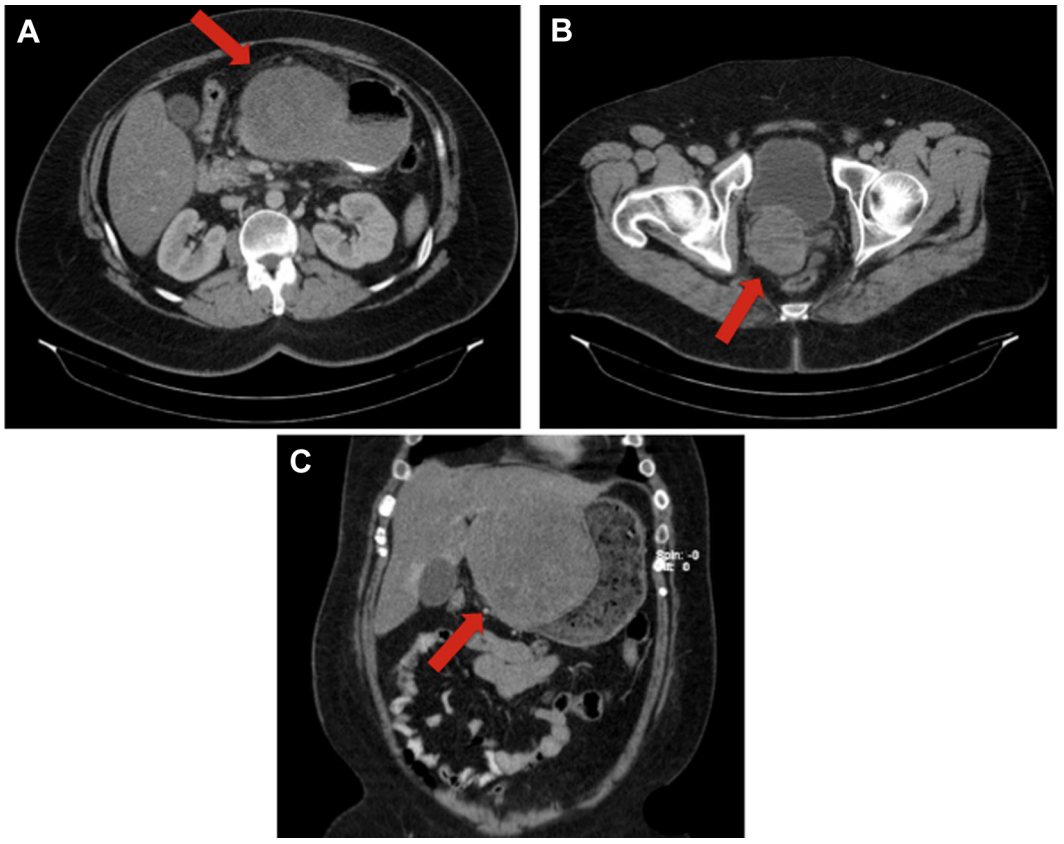

Figure 1. CT abdomen/pelvis on initial presentation, axial (A,B) and coronal (C). These images demonstrate the duodenal mass (A, C), and the pelvic mass (B), which were identified at presentation, the red arrows point to the "duodenal mass," and "pelvic mass".

8.4 × 7 × 5.6 cm to 10 × 8 × 8.1 cm, and multiple new liver metastases (Fig. 3A). The pelvic/retroperitoneal mass was consistent with growing teratoma syndrome (GTS).[3] Additionally, the patient developed myelodysplasia secondary to treatment, with severe thrombocytopenia (Platelet counts < 5000). MRI of the pelvis was performed for surgical planning (Fig. 3B). Despite his severe thrombocytopenia, he underwent extirpation of the pelvic/retroperitoneal growing teratoma, right seminal vesicle, and right distal ureter. Concomitant psoas hitch and ureteral reimplantation was performed. Pathologic analysis demonstrated mature teratoma, consistent with GTS. The patient had an uncomplicated immediate postoperative course and was discharged home on postoperative day five. Unfortunately, the patient continued to experience progressive bone marrow suppression, and was unable to receive further therapy. Patient died secondary to progression of his disease and severe bone marrow suppression 5 months later.

Discussion

Extragonadal germ cell tumors have been identified in a variety of anatomical locations.[1,4] Incidence of EGCT in abdominal viscera, such as the duodenum, is very rare.[1] Unfortunately, there is very little referenced in the literature about abdominal visceral EGCT. Knowledge is therefore extrapolated from mediastinal and retroperitoneal EGCT, which are the most common sites of disease. As compared with seminomatous EGCT, nonseminomatous ECGT have worse prognosis, with a 5-year survival rate of 62% for retroperitoneal and 45% for mediastinal.[1] Presence of a nonpulmonary visceral metastasis or primary tumor location other than testicle

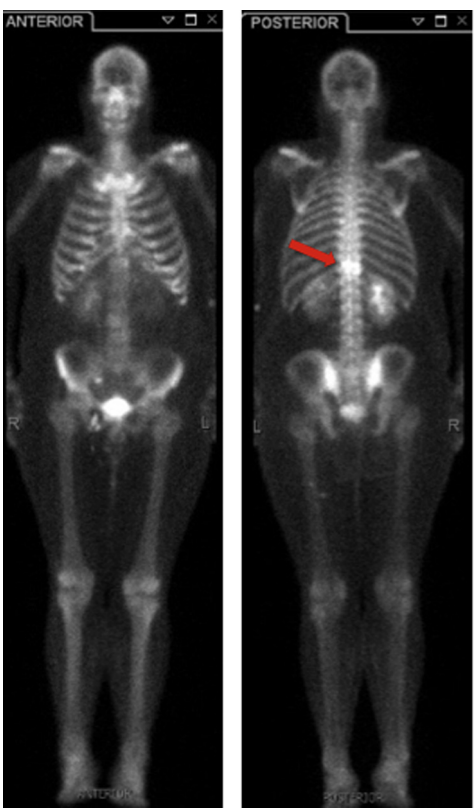

Figure 2. Bone scan demonstrating T11 lesion, the red arrow points to the "T11 lesion".

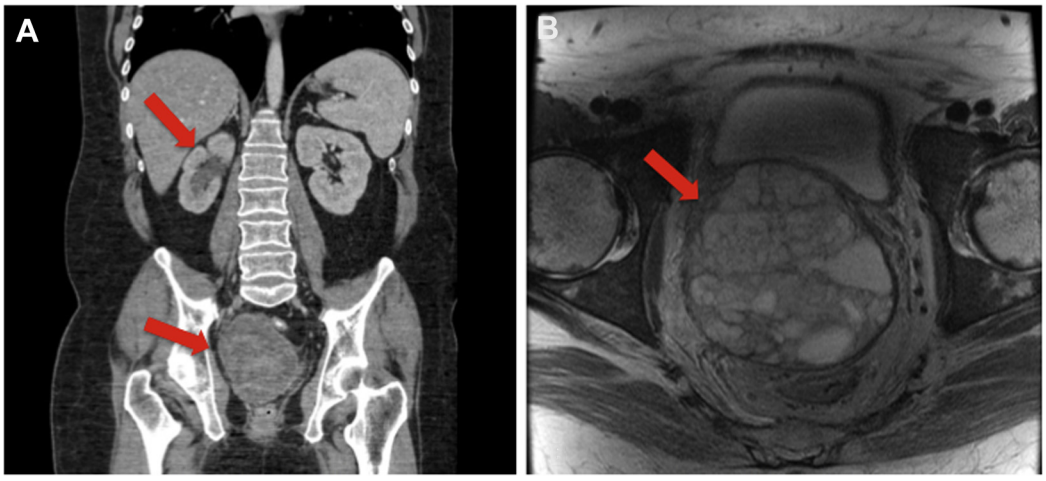

Figure 3. CT (A) and MRI (B) after BEP × 4 cycles, demonstrating growing teratoma the red arrows point to the "growing teratoma".

and retroperitoneum automatically places a patient in the International Germ Cell Cancer Collaboration Group (IGCCCG) classification of poor prognosis. This group has a 5-year survival rate of 48%.[5] Surgery is an integral component of treatment of EGCT due to the risk of residual viable tumor. In one series, after secondary surgery, 25% of patients with nonseminomatous retroperitoneal EGCT had viable undifferentiated tumor in the specimen, and 16% had major teratoma.[1] Additionally, surgical excision is the treatment of choice in the setting of GTS. GTS is defined as enlarging retroperitoneal mass or metastatic lesion during systemic chemotherapy for NSGCT, with normalization of tumor markers, and predominance of mature teratoma in resected specimen.[3] In cases with partial remission or disease progression after resection, there is a role for salvage chemotherapy. The median survival time for patients requiring salvage chemotherapy after relapse was 11-15 months.[1]

In addition to the poor prognostic factors, the patient also developed myelodysplasia with severe thrombocytopenia and bone marrow suppression. Patients with nonseminomatous mediastinal EGCT have a known increased risk of developing acute megakaryoblastic leukemia and myelodysplasia with abnormal megakaryocytes.[1] This is seen in 2% of patients, which is 250 times greater incidence as compared to the general population.[1] After development of hematologic malignancy, median survival is approximately 5-6 months despite efforts to treat.[1] We intended to perform further site-directed excisions of his likely multiple growing teratomas after improved control of his thrombocytopenia and possibly salvage chemotherapy. Unfortunately, the patient was never able to tolerate these treatments, and succumbed to complications of his disease 5 months after surgery.

Conclusion

We report a rare case of EGCT and GTS in a male with KS who initially presented with a duodenal mass, which has not been described in the literature. Unfortunately in this patient with GTS, he was unable to reach complete resection due to severe complications of chemotherapy and of his disease, ultimately resulting in his death.

Conflicts of interest

None.

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